24%, at least about 25%, at least about 26%, at least about 27%, at least about 28%, at least about 29%, or at least about 30%.

[0070] In some exemplary embodiments, the protein can be a naturally occurring protein.

[0071] In some exemplary embodiments, the protein can be a recombinant protein.

[0072] In some exemplary embodiments, the protein can be a bio-therapeutic protein.

[0073] In some exemplary embodiments, the protein can be a recombinant protein, wherein the recombinant protein can be a trap protein, a chimeric receptor Fc-fusion binding molecule, a chimeric protein, an antibody, monoclonal antibody, a polyclonal antibody, a human antibody, a bispecific antibody, an antibody fragment, a nanobody, a recombinant antibody chimera, a cytokine, a chemokine, or a peptide hormone.

[0074] In some exemplary embodiments, the protein can comprise modifications, adducts, and other covalently linked moieties.

[0075] In some exemplary embodiments, the protein can comprise a post-translational modification.

[0076] The consecutive labeling of method steps as provided herein with numbers and/or letters is not meant to limit the method or any embodiments thereof to the particular indicated order.

[0077] Various publications, including patents, patent applications, published patent applications, accession numbers, technical articles and scholarly articles are cited throughout the specification. Each of these cited references is incorporated by reference, in its entirety and for all purposes, herein.

[0078] The disclosure will be more fully understood by reference to the following Examples, which are provided to describe the disclosure in greater detail. They are intended to illustrate and should not be construed as limiting the scope of the disclosure.

EXAMPLES

[0079] To study the contents of a cell culture medium and its effect on the production of a protein, cell culture comprising soy hydrolysate was selected for generating a VEGFR binding protein 1.

Example 1

[0080] Soy hydrolysate content analysis was performed using nine different lots obtained from three distinct shipments—1, 2 and 3. The samples from these three distinct shipments were sent to Metabolon (Durham, N.C., USA). The soy hydrolysate content analysis was conducted at Metabolon using liquid chromatography-mass spectrometer. Over three hundred components in the soy hydrolysate were measured. Only the results scaled to median were provided.

[0081] For studying the effect of biochemicals on the titer of VEGFR (Vascular Endothelial Growth Factor Receptor) binding protein 1, an orthogonal partial least squares (OPLS) model was used for multivariate analysis (MVA). Seventy soy hydrolysates lot were included in the study.

[0082] The dependence between the components and titer was evaluated by studying the correlation and covariance. A positive dependence suggests an increase in titer with increase in the biochemical and a negative dependence suggests a decrease in titer with increase in the biochemical. For the final titer evaluation for a principal component, the values for R^2X, R^2Y and Q^2 were found to be 0.315, 0.672, and 0.493, respectively. The components that showed positive dependence are shown in Table 1 and the components that showed negative dependence are shown in Table 2.

TABLE 1

Positive dependence
Nicotinamide
Lactate
phenyllactate (PLA)
5-methylthioadenosine (MTA)
Indolelacate
Succinate
alpha-hydroxyisocaproate
3-(4-hydroxyphenyl)lactate (HPLA)
alpha-hydroxyisovalerate
2-hydroxy-3-methylvalerate

TABLE 2

Negative dependence
Nicotinate
Sucrose
Uracil
Phenylalanine
Valyleucine
Maltose
digalactosylglycerol
pantothenate (Vitamin B5)
Xanthine
Serine

[0083] The MVA result normalized to unit length is shown in FIG. **1**. Based on these finding from example 2, nicotinamide and 5-methythioadenosine were selected as positive markers for further analysis.

Example 2

[0084] The impact of 5-methythioadenosine on production of a recombinant protein (VEGFR binding protein 1) was studied by investigating the protein titer (g/L) at different concentrations of 5-methythioadenosine present in the cell culture medium.

[0085] An enriched medium (soy hydrolysate) comprising 5-methythioadenosine was added to the cell culture medium. FIG. **2** shows the correlation between the concentration of 5-methylthioadenosine present in the soy hydrolysate added to the cell culture medium with the titer of VEGFR binding protein 1.

[0086] As seen in FIG. **2**, the regression line relating to the variables (N=70) extrapolated suggests that titer varied linearly to the concentration of 5-methythioadenosine in the soy hydrolysate added to the cell culture medium, suggesting that higher titer can be obtained on increasing 5-methythioadenosine concentration in the cell culture medium.

Example 3

[0087] Based on the correlation data obtained from studying the effect of 5-methythioadenosine concentrations in the enriched medium (soy hydrolysate) supplemented to the cell culture medium (Example 2, FIG. **2**), an estimation as to the optimum concentration of 5-MTA in a cell culture was made. FIG. **3** shows the regression line relating to the